Familial Adenomatous Polyposis

SBS11QHG-06
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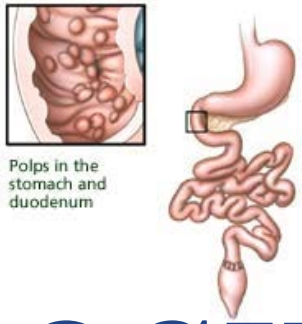
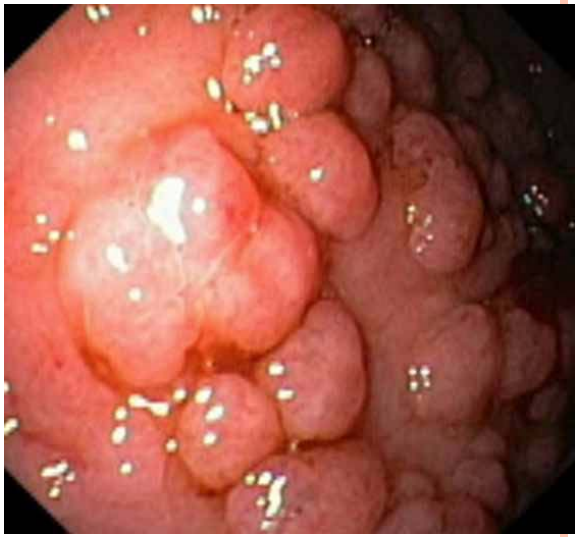
PERIOD 6 #9

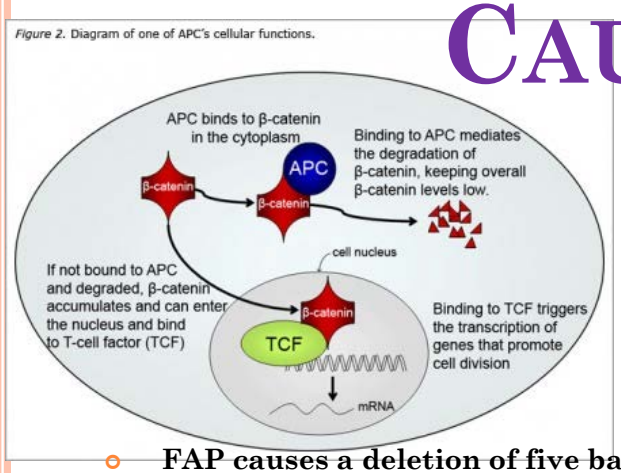


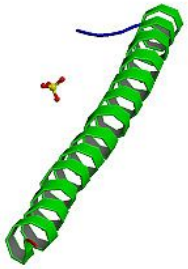


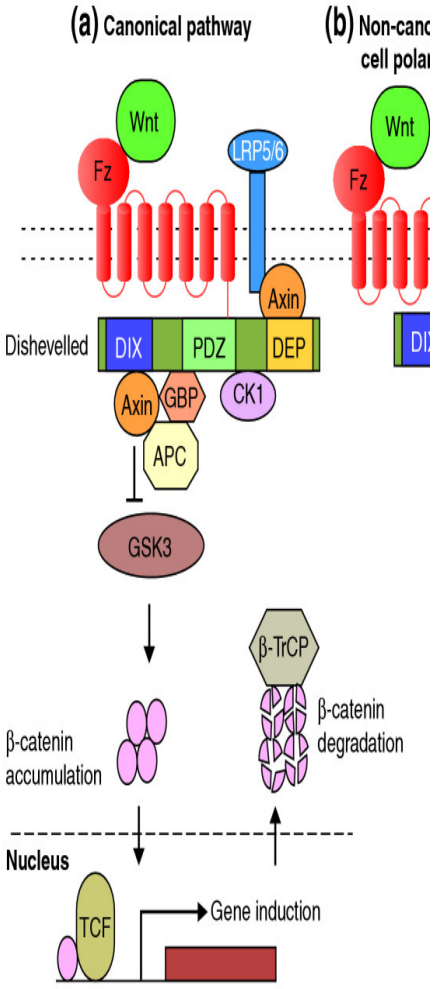
PHYSIOLOGY

- The colon plays one of the most important roles in the body, extracting salt and water from the wastes and eventually creating fecal matter.
- Familial Adenomatous Polyposis (FAP) occurrence ranges from 1 in every 7,000 people to 1 in every 22,000. It is more commonly found in Western Populations.
- The age of onset usually varies from age 7 to age 40 and at age 40 and since FAP is a colorectal cancer, there is a strong risk of it (at age of 40) destroying the entire digestive tract.
- Even though, 70% of cases show that it is a result of family history, the other 30% are all sporadic cases where the mutation simply occurs.
- FAP is an autosomal dominant disease thus allowing the easy readings of family history (if a parent is homozygous then the child will have it 100%). It is also not gender specific and is a Mendelian type of disease.
- The major symptom of FAP is the development of polyps which are an abnormal growth of tissue on the lining of the colon which eventually will lead to colon cancer. These polyps are also known as adenomas (meaning they are precancerous).
- Due to the spread of the polyps other symptoms include: colorectal cancer, pancreatic cancer, stomach cancer, bleeding from the rectum due to the tissue overgrowth, huge change in bowel habits, and abdominal pain.

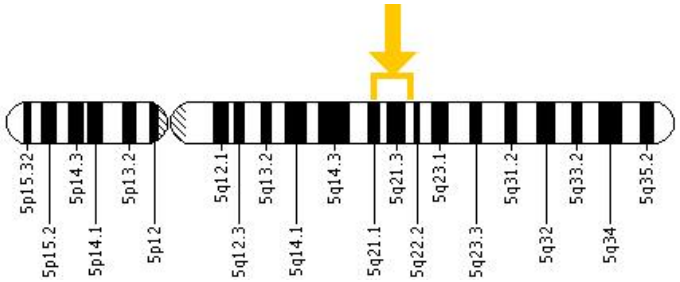
Molecular Cause



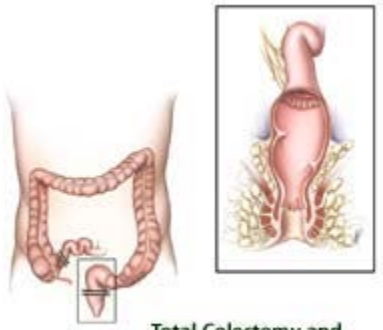




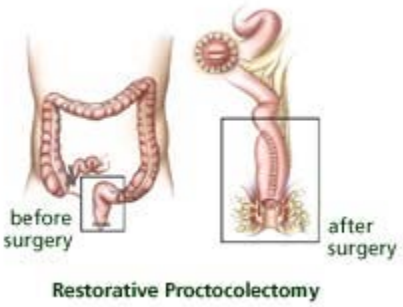
- **FAP causes a deletion of five bases on the APC gene (adenomatous polyposis coli) located between 5q21 and 5q22. This essentially causes a shortening of the APC protein leading it to fail its role in the canonical pathway.**
- **The canonical pathway occurs in the tissue of the lining of the colon cells. It is a type of Wnt-1 signaling pathway. The Wnt signaling pathways are a group of signal transduction pathways made of proteins that pass signals from outside of a cell through cell surface receptors to the inside of the cell essentially leading to the production of cells on the lining of the colon.**
- **The APC protein works hand in hand with GKS3 (glycogen synthase kinase 3) and is responsible for the degradation of Beta-catenin. The APC gene is also a tumor suppressor gene responsible for the controlled growth of cells. However, due to FAP the APC protein is truncated and becomes too short to attach the GKS3 at the binding sites leading to a fail regulation o Beta- Catenin. Beta- Catenin begins to over-accumulate and then enter the nucleus where it binds to T cell factor 4 and wrongly activates the expression of cell proliferation and causes uncontrolled cell growth.**
- **Due to this uncontrolled cell growth, polyps or the tissues begin to form along the germ lining of the colon.**



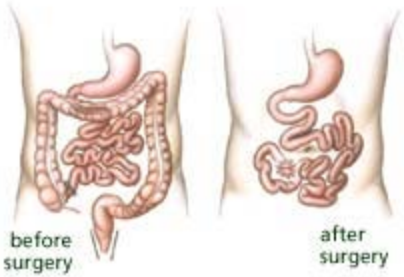
TREATMENT AND CURRENT LIMITATIONS



Total Colectomy and Ileorectal Anastamosis



Restorative Proctocolectomy



Proctocolectomy and Ileostomy

The most current technique to finding out whether you have or not is family history due to it being autosomal dominant.
However, since 30% of cases are sporadic screening at a young age either Sigmoidoscopy or colonoscopy to look and see if there is a development of polyps.
Current treatments and therapies for it are chemotherapy where they target the polyps on the colon and the use of drugs such as sulindac and celecoxib.
There is also a “cure” in removing cancerous parts of the colon and rectum and create a new sort of bowel system.
The three most done are a colectomy, proctocolectomy, and ileostomy.
The drawbacks being the radiation, the formation of desmoid tumors after the surgery, and (after a ileostomy) having to use a bag as a bowel/ waste remover. Of course, drugs all have their side effects.

Proposal and limitations

- Due to the fact that tumors can still arise after the surgery and the only thing sulindac can do is remove the polyps I propose having a physical method of eliminating the problem and a non-viral in vivo direct method.
- With technology developing even further, lasers would soon be able to treat polyps on a much greater and more effective scale than that would chemotherapy. It would target the uncontrolled cell growth and eliminate the polyps. However, the accuracy and whether or not it will destroy any parts of the colon is unsure of.
- I also believe that with laparoscopy on the rise (which is an incision in the abdomen to look at the colon) it could be possible to create new medication (that would work the same way as sulindac which kills the polyps) and put it into either a liquid or sort of gel form and spread it along the colon to simply destroy the cell growth before it even begins.
- The in vivo method or within, would involve using micelles (which is a liquid colloid containing both hydrophobic tails and head to allow passage through the membrane. Inside would either be a new APC protein that we would have created either from mice or other humans or a proper APC gene to direct the functions and create the APC protein. To target the specific area this could be done by either a gene gun (particles being the DNA or protein are accelerated to sufficient velocity by highly pressurized inert gas) to the target tissue or a hydrodynamic method (which currently isn't used or been tested for the colon) or a jet injection (uses pressure to send it directly to the target tissue and this method has been used to directly transfect skin cancer cells to facilitate conventional chemotherapy so it needs to be tested to be worked with colon cells) to help fix this problem. We could also directly inject topical medication into the bloodstream, however, it would mean the whole body would receive it.

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